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History and clinical signs

A 10-month-old, neutered female Doberman was referred to the dermatology referral service at the Ontario Veterinary College for evaluation of alopecia that started at 5 mo of age with a patch of alopecia on the dorsal midline at the withers. The initial lesion had progressed in size with the development of additional lesions over the dorsal thoracic lumbar region. The owner described the dog as being only sporadically pruritic. Skin scrapings performed by the referring veterinarian were negative for *Demodex canis*. The dog had been treated with levothyroxine (Synthroid; Abbot Laboratories, Saint-Laurent, Quebec), 0.3 mg, PO, q24h for 3 mo, on account of her having a low total T3 but normal T4, without improvement. At the time of referral, the only therapy the dog was receiving was periodic bathing with a moisturizing shampoo (Allergroom; Virbac, St Lazare, Quebec).

On presentation, multicentric irregular patches of alopecia, 1.5 to 6 cm in diameter, were noted to be affecting the trunk (Figure 1). Pruritus was not noted at this time.

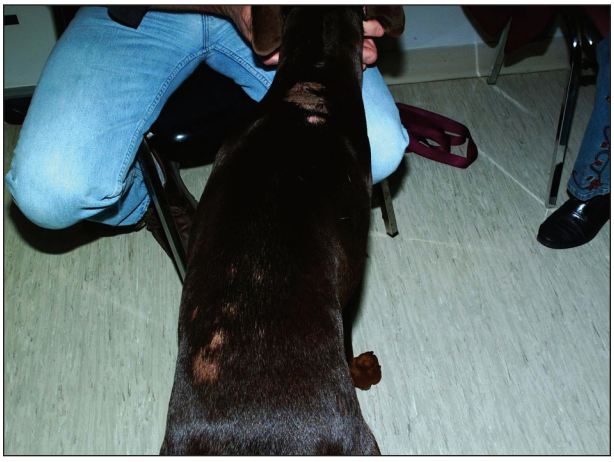

Figure 1. Multifocal areas of alopecia over the dorsal aspect of the trunk of a 10-month-old Doberman.

What is your clinical diagnosis and therapeutic plan?

Differential diagnoses for patchy alopecia affecting the trunk would include demodicosis, dermatophytosis, superficial pyoderma, hypothyroidism, and follicular dysplasia. Based on the age of the dog and the clinical presentation, multicentric juvenile onset demodicosis was suspected.

Multiple trichograms were negative for *Demodex canis*. Skin scrapings taken from 5 areas of hair loss revealed 3 adult *D. canis* mites on a scraping from the lumbar region, and 1 adult mite with 2 to 3 eggs on a scraping taken from the thoracic midline. The other skin scrapings were negative. A complete blood (cell) count, serum biochemical profile, urinalysis, and total T4 evaluation with endogenous TSH revealed no significant abnormalities. Multiple skin biopsies, representing the range of clinical lesions, were performed under sedation with medetomidine (Domitor; Novartis, Mississauga, Ontario). Eight skin biopsies were taken with a 6-mm biopsy punch from alopecic and thinly haired areas over the dorsal and ventral trunk. In all sections examined histologically, mural folliculitis was prominent, characterized by lymphocytic infiltration of the follicular epithelium. *Demodex canis* mites were seen in most hair follicles, with disruption of the outer follicular epithelium, hydropic degeneration and apoptosis of keratinocytes, and pigmentary incontinence of the perifollicular dermis (Figure 2). Rare follicles had ruptured (furunculosis) and were surrounded by perifollicular granulomas composed of histiocytes, plasma cells, and lymphocytes. Mural folliculitis is a consistent lesion associated with clinically relevant cases of demodicosis (1). Granulomas persist longer than mural folliculitis and may be the only lesion seen on biopsies of resolving clinical cases.

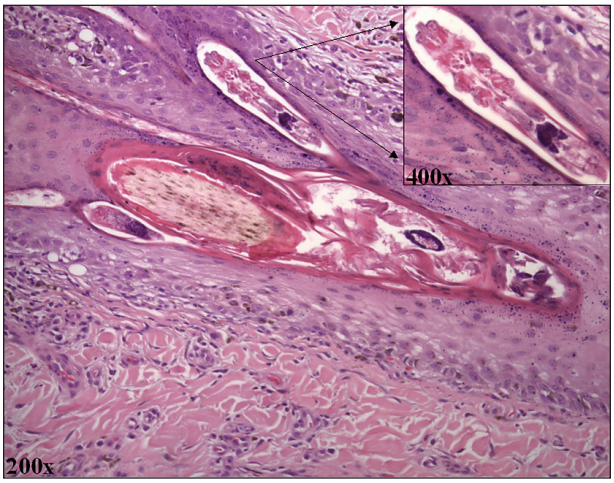

Figure 2. Photomicrograph of the skin from a 10-month-old Doberman (200×). Multiple *Demodex canis* mites are to be noted within a hair follicle, with associated mural folliculitis. A closer view (400×) of 1 mite is shown in the upper right inset.

As examination of the skin scrapings suggested that the demodicosis was resolving without therapy, it was decided not to treat the condition initially. Shampoo

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therapy with benzoyl peroxide (Pyoben; Virbac) once weekly, followed by a soothing conditioning oatmeal rinse (Resisoothe; Virbac) was instituted.

At reevaluation 4 wk later, some hair growth was noted. Multiple trichograms revealed only 2 adult *D. canis* mites. Multiple skin scrapings from areas of hair loss were negative. The owner was advised to continue with the shampoo therapy until the next visit.

Four weeks later, the patches of hair loss were still present and a papular eruption had developed over the dorsal aspect of the trunk. Five *D. canis* mites were found on 4 skin scrapings. Therapy with ivermectin (Ivomec, 10 mg/mL; Merial, Baie d'Urfe, Quebec) was instituted. To allow monitoring for side effects indicative of ivermectin toxicity (mydriasis, ataxia, weakness, hypersalivation), a gradually increasing dosage schedule was utilized starting at 0.05 mg/kg bodyweight (BW), PO, q24h on day 1, increasing to 0.12 mg/kg BW (the "test dose" in sensitive collies), PO, q24h for 7 d, 0.2 mg/kg BW, PO, q24h for 7 d, then increasing incrementally by 0.1 mg/kg BW every 7 d until the treatment dose of 0.6 mg/kg BW, PO, q24h was reached. The dog was also treated with cephalexin (Novolexin; Novopharm, Toronto, Ontario), 30 mg/kg BW, PO, q12h for 8 to 12 wk, pending reevaluation. The shampoo therapy was continued.

At a reevaluation 4 wk later, the hair had continued to grow in all areas. Multiple skin scrapings were negative for *D. canis*. The ivermectin therapy was continued for a further month. Monthly reevaluations, over a further 2 mo, confirmed an excellent response to the ivermectin, with full hair regrowth and negative skin scrapings. The dog was gradually weaned from the ivermectin over a period of 3 mo, while monitoring for signs of relapse. Six months later, the dog continues to do well without relapse.

Discussion

Demodex canis is a normal resident of dog skin and is present in small numbers on most healthy dogs (2). The cigar-shaped mite lives in the hair follicles and sebaceous glands and feeds on epidermal debris and sebum. There are 4 different stages in the mite life cycle. Eggs hatch into 6-legged cigar-shaped larvae that moult into an 8-legged nymph stage and then into 8-legged adults. Transmission occurs from bitch to pups in the first 2 to 3 d of life. The condition is not considered to be contagious.

Whether a dog develops demodicosis depends on immunological factors that are affected by genetic influences (2). The mites can seize the opportunity to proliferate if immunological tolerance develops. In adult dogs, changes in the immune system relating to internal systemic disease allow the mites to proliferate. Estrus, vaccination, heartworm infection, and corticosteroid therapy can potentially aggravate *D. canis* infections. Because demodicosis has a genetic component, affected individuals should not be bred. The presence of secondary pyoderma may aggravate the demodicosis by contributing further to immune suppression.

Two forms of demodicosis are recognized, a localized form and a generalized form. Localized demodicosis typically presents as 1 to 3 small areas of patchy alopecia, mild erythema, and scaling on the face or forelegs. Generalized cases have more extensive involvement, although, as in this case, only patches of hair loss may be noted. Erythema, alopecia, scaling, and plugging of hair follicles may be noted. Pruritus may be observed, especially in generalized cases that present with erythema. As pruritus may be seen in some demodicosis cases, demodicosis must be considered as a differential diagnosis in cases of pruritus. Electing to use steroids in a suspected pruritic pet without ruling out *D. canis* infestation may have a significant impact on the progression of the condition. Generalized demodicosis may be associated with the development of a severe secondary folliculitis and furunculosis, which may further suppress the immune system, allowing further mite proliferation. Pododermatitis is also common, often complicating quick recovery because of persistent mite infestation and resulting fibrosis (3).

Although most cases of demodicosis occur in puppyhood, infection can develop in older animals. In these cases, late- or adult-onset demodicosis normally accompanies internal disease or immunosuppressive therapy. Adult-onset demodicosis is interesting, because, in many cases, no obvious internal disease can be found at the time the demodicosis is diagnosed, despite extensive investigation. However, within 1 to 2 y, severe internal disease develops. In all cases, the prognosis is guarded.

Diagnosis of demodicosis is normally based on skin scrapings or hair plucks (trichograms) from affected areas. Scrapings from 4 to 5 sites on the body are normally taken. Prognosis is normally based on the ratios of eggs and larval forms to adults, as well as the number of live to dead mites. Generally, the larger the number of juvenile forms, the worse the prognosis. As treatment progresses, increased numbers of dead mites and decreased numbers of juvenile stages would indicate a favorable prognosis. Scrapings, hair plucks, or both are normally performed periodically during therapy. A skin biopsy may be used to make a diagnosis in cases affecting the feet (pododermatitis) and in shar-peis, where, because of the thickness of the skin, the follicles extend deeply, making it harder to find the mites on skin scrapings.

Demodicosis can be a challenging condition to treat. Most cases of localized demodicosis will resolve themselves as the immune system of the puppy matures. If treatment of the localized form is desired, the use of a benzoyl peroxide gel to flush the hair follicles or focal use of an amitraz dip (Mitaban; Pfizer, Montreal, Quebec) can be employed. Self-cure is believed to occur because the immune system, as it matures, is finally able to suppress the growth of the mites and bring mite numbers under control. In cases that become generalized, the immune system never fully develops resistance to the mites, immunologic tolerance develops, and the mites are allowed to proliferate and spread.

Currently, the most common therapy for generalized demodicosis is ivermectin, 0.3 to 0.6 mg/kg BW, PO, q24h (4,5). The cure rate in most studies is higher at the 0.6 mg/kg BW than at the 0.3 mg/kg BW dose rate. Progress should be reevaluated by skin scrapings or trichograms every 4 wk during therapy. After clinical cure has been achieved, the dog is gradually weaned off

the medication by decreasing the dose frequency to every 2nd d for 1 mo, every 3rd d for 1 mo, and then once weekly for 1 mo. Resistance issues or the risk of relapse is minimized by an intensive treatment program.

Dogs receiving ivermectin therapy should be monitored carefully for signs of neurotoxicity. Clients should be briefed about the signs to watch for (mydriasis, ataxia, weakness, hypersalivation etc) and risks (coma and death) prior to therapy. Although toxicity can occur in any breed, collies and collie crosses are most at risk. Testing for the presence of the *mdr-1* mutant gene responsible for ivermectin toxicosis is available (6). This gene encodes for P-glycoprotein, which is responsible for exporting many drugs and other toxins out of the brain. Dogs with the mutant gene cannot pump the ivermectin out of the brain, resulting in the accumulation of ivermectin and the development of neurological signs. Approximately 3 of every 4 collies in the United States are believed to have the mutant *mdr-1* gene (7). Initial studies have shown that the frequency is about the same in France and Australia, so it is likely that most collies worldwide have the mutation (7). The mutation is present in other herding breeds, but at a lower frequency than in collies.

Ivermectin sensitivity testing is available at the Washington State University College of Veterinary Medicine, Veterinary Clinical Pharmacology Laboratory, (Phone/FAX 509-335-3745, VCPL@vetmed.wsu.edu). A cheek brush sample is required for analysis.

Milbemycin (Interceptor; Novartis), 1 mg/kg BW, PO, q24h, increasing to 2 mg/kg BW if no improvement is noted after 4 wk, and moxidectin (Cydectin Injection, 10 mg/mL; Wyeth) 0.4 mg/kg BW, PO, q24h, are alternatives to the use of oral ivermectin (2,8).

Amitraz (Mitaban; Pfizer), a monoamine oxidase inhibitor and a2-agonist, is the only approved therapy for demodicosis. Because of concern regarding side effects (transient sedation, depression, lethargy, pruritus, gastrointestinal upset, and hyperglycemia in diabetics, and the risk to the operator, it is less frequently used. Amitraz should always be handled by wearing gloves in a well-ventilated area.

Amitraz has a reported cure rate of 0 to 99%, depending on study and protocol used (4,5). At the Ontario Veterinary College, a protocol of 8 weekly dips, followed by 2 every other week dips, and 2 monthly dips (12 dips in 20 wk) is recommended. Medium-sized dogs (5 to 15 kg) are treated at the label recommendation of 250 ppm or 0.025%. For small dogs ($<$ 5 kg), only half the dog is treated at a time to minimize the risk of side effects. Large dogs ($>$ 15 kg) may be treated at twice the strength indicated on the label (500 ppm or 0.05%). To avoid relapses and resistance, and to ensure that the product is given time to work, all patients should receive the full treatment program. Skin scrapings and trichograms are performed once every 4 wk during therapy.

Benzoyl peroxide shampoos are especially useful in the treatment of generalized demodicosis because of their follicular flushing ability. The use of vitamin E 200 IU (up to 5 times/d) and nonspecific immunomodulators remains critically unproven. If they are being considered, they should form part of an overall treatment plan. As pyoderma may be a significant secondary problem, antibiotic therapy should be continued for 4 to 12 wk, depending on response.

This case highlights the fact that demodicosis can be a challenging diagnosis to make in some cases. Biopsy should be considered if mites are difficult to find on scrapings, especially where the clinical signs are typical. The key to a successful outcome is early recognition, followed by appropriate and thorough treatment.

References

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